THE EFFECT OF COMMUNITY-BASED NUTRITION PROGRAMS ON CANCER-RELATED BIOMARKERS IN PEOPLE WITH CANCER

by

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THE EFFECT OF COMMUNITY-BASED NUTRITION PROGRAMS

ON CANCER-RELATED BIOMARKERS IN PEOPLE WITH CANCER

A Thesis for the Degree of

Master of Science in Kinesiology

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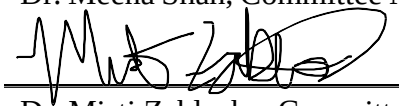

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ABSTRACT

This study looked at a community-based nutrition intervention in a cancer population. Participants were supplied seven meals a week for the total study duration of 6-weeks. Participants had blood drawn via venipuncture and finger stick. Pre- and post-intervention serum levels of inflammatory cytokines and lipid panel markers. QOL questionnaires assessed participants cancer symptoms, including fatigue, were affecting their physical and social habits. Overall, while no significant changes were seen, the results showed positive trends in self-reported fatigue, health limiting activities, and lipid panel markers. These results can be used as preliminary evidence to support further studies that investigate the use of community-based nutrition interventions for people with cancer. Future research can focus on larger studies that include longer interventions, and look at more specific populations regarding cancer type, sex, or ethnicity.

Chapter 1. Introduction

Cancer is one of the leading causes of death worldwide. There were 19.3 million new cases and almost 10 million deaths in 2020 alone.[1] Cancer can be devastating to one's health, but also may have significant financial implications. Personal health care cancer costs were $115.4 billion in 2013, with estimates close to $200 billion in 2020. Financial toxicity refers to the financial burden on a patient's outcomes and quality-of-life (QOL).[2] Unfortunately, financial toxicity can continue to harm patient's, even after they may be in remission or done with cancer treatments. There are also psychosocial implications of cancer, where diagnosis and treatment may impact a patient's well-being. Such mental impacts may stem from loss of employment, financial strains, as well as physiological changes. For example, there is an association between elevated inflammatory markers and depression in cancer patients. Cytokines are some of the most studied biomarkers in patients with cancer, and have been shown to be elevated in this chronic disease state.[3] Research on exercise and nutrition interventions in patients with cancer has been associated with favorable outcomes in future prognosis, treatment completion and reducing cachexia and other related toxicities.[4-6] Additionally, many patients diagnosed with cancer also suffer from other comorbidities such as COPD, type-2 diabetes, chronic infections, hypertension, or hyperlipidemia,[7]. Due to these comorbidities it is also important to monitor traditional cholesterol panel biomarkers that include; high-density lipoprotein, low-density lipoprotein, and triglycerides. Based on laboratory research, organizations have developed community-based programs to help address lifestyle behaviors in patients with cancer that may improve levels of the above-mentioned biomarkers. Prior research has shown community-based interventions that provide engagement have improved health screening and awareness. For example, community awareness increases screening for colorectal cancer.[8] The use of

community-based programs can also help provide care and resources for patients with a lower socioeconomic status.[9-10] However, more research is needed to study the effects of these community-based exercise and nutrition interventions in a population with a cancer diagnosis.

Because of their physiological involvement in cancer, cytokines are one of the most important variables in the body's response to cancer. Cytokines are secreted proteins important for the information communicated between different cells.[11] This relationship between cancer and cytokines becomes even more important during cancer treatment. Cytokines can be used to measure inflammation changes throughout the cancer process and during treatment. Several cytokines have also been studied as cancer immunotherapies. Research on cytokines as cancer treatments has only just started, but several cytokines including interferon-alpha (IFN-α), interferon-gamma (IFN-γ), and interleukin-2 (IL-2) have been approved to be used clinically in anticancer treatments. Others such as interleukin-12 (IL-12), interleukin-15 (IL-15), and interleukin-21 (IL-21) are in ongoing research for potential therapeutic use.[12] To understand how cytokines may be useful or harmful in the progression of cancer, it is important to know their role at the cellular level. When the body encounters a pathogen, infection, or injury; white blood cells produce cytokines to help regulate the immune response. These cytokines trigger immune cells and the release of other cytokines to help the body defend itself.[13] Cytokine levels are higher in the presence of disease, including cancer, due to the role they play in the tumor microenvironment. There has been some research on the potential of using cytokine levels to help with earlier detection of cancer.[14] It is important to understand how diet and exercise affect the immune process as well.

Diet and exercise are two factors that both affect the inflammatory process. During exercise, the molecular damage of the muscle tissue leads to an acute immune response and

changes in circulating biomarkers. This acute inflammatory process from exercise can last up to 24 hours, followed by a regenerative response. Circulating cytokines are measures of current inflammation and have been shown to be elevated in a chronic disease state. The immunologic adaptations from the acute inflammatory process, may help explain some of the long-term benefits of exercise.[15] Benefits have already been found in a cancer population. Just 15 minutes or more of daily moderate intensity activity has been associated with positive effects on cancer mortality.[16] Exercise has also become increasingly commonplace as part of cancer treatment and rehabilitation. Following surgery for lung cancer, exercise rehabilitation has been associated with decreased postoperative complications and pulmonary complications.[17] Adequate nutritional status is important for the regulation of immune and oxidative processes. Poor nutritional status has been associated with an increased risk of infection.[18] However, more research is needed to study various exercise modes, intensities, and durations and their immunologic effects. More research is also needed on biomarker changes following nutritional interventions. This is particularly important, due to the devastating physiological effects cancer treatment can have on an individual.

Cancer immunotherapies have seen a large amount of development in the last few decades, which has had an enormous impact on the survival rates in many types of cancers. However, many cancer treatments are still not without the risk of toxicity. Although treatments can help kill malignant cells, patients often feel extensive side effects. Immune checkpoint inhibitors have shown momentous results on mortality in metastatic cancer by controlling the cancer cell's effect on the T cell response. However, they have also been associated with many cardiovascular toxicities. Those receiving immune checkpoint inhibitor treatment, especially those with a heart history or receiving combination immunotherapy, are at an increased risk for

myocarditis, vasculitis, arrhythmias, or other cardiovascular based toxicities.[19] Radiation therapy is also frequently used to treat most types of solid tumors. Although treatment works to kill as much of the cancer cell with the least amount of surrounding cellular damage, patients are at risk for many adverse effects. Fibrosis, cognitive dysfunction, pneumonitis, hematologic suppression, hair loss, and gastrointestinal are a few of the toxicities that radiation therapy may cause. Radiation also has carcinogenic potential itself, with increased risk seen with increased time of exposure.[20]

Patients undergoing chemotherapy may also be at risk of developing symptoms of cachexia. Cancer cachexia has also been associated with the development of further toxicities. More research should focus on the effects of these conditions on patient outcomes in different cancer types.[21] Cachexia is associated with cancer morbidity and mortality. Cachexia progression has been associated with increased systemic inflammation and poor nutritional status. Chronic elevation of inflammatory cytokines correlates with skeletal muscle and tissue dysfunction. Exercise has shown promise as an intervention for preserving muscle mass, improved metabolic function, and mediating inflammatory cytokines. Current research suggests multimodal approaches, with inclusion of exercise, nutrition, and cancer treatment intervention, are needed to see the best outcomes in patients with cachexia. However, further research should focus on the potential magnitude and mechanisms of these treatment models.[22] This is also the best way to improve QOL measurements in patients with cancer.

The effects of cancer itself and cancer treatments can potentially impact not just an individual's physical health, but also emotional, social, and cognitive function.[23] Choosing cancer treatment options for patients can involve consideration of factors such as age, prognosis, and family circumstances. Systematic reviews of QOL in patients with cancer demonstrate the

complexity of choosing QOL versus length-of-life. While patients frequently feel that QOL and length-of-life are equally important, baseline QOL and future expectations seem to be the key determinants when assessing treatment options.[24] This is why exercise and nutrition programs are so important for improving QOL measures and potentially future prognosis. Supervised and home-based physical activity programs have showed some ability to reduce perceived fatigue in patients undergoing chemotherapy or radiation therapy treatments.[25] Moderate to vigorous physical activity has also been associated with higher health-related QOL in colorectal cancer survivors. This association was mediated by fatigue and distress, demonstrating the importance of measuring fatigue when QOL is considered.[26] Fatigue is just one of many QOL related symptoms that can interfere with the dietary habits of a patient with cancer. Symptoms that can cause difficulty maintaining adequate nutritional intake can include; fatigue, anorexia, vomiting, diarrhea, or difficulties with taste, smell, or swallowing. These can be considered nutrition impact symptoms, which contribute to the metabolism dysfunction associated with cancer cachexia.[27] Fatigue and anxiety can also be a barrier to engagement in healthy lifestyle behaviors, including nutrition. Research focusing on nutrition interventions can help provide ways to improve fatigue and subsequently other QOL measures.[28]

Additionally, nutrition therapy during and after cancer treatment can also help improve patient's lipid profiles.[29] Research on the role of lipid profiles in patients with cancer is paramount to further understanding how to improve the health of patients with cancer. Lipid profile alteration may be in part due to tumor pathogenesis, as well as lifestyle factors.[30] While abnormal lipid profiles have been frequently demonstrated with patients with cancer, their role in cancer is still ambiguous. Because of this the clinical significance of lipid profiles in cancer risk stratification needs further study.[31] Investigation of lipid profiles in patients with cancer has

shown a correlation between increased low-density-lipoproteins (LDL), and metastasis across breast, colon, gastric, and ovarian cancer.[32] Lipid profiles may also be altered when undergoing cancer treatment. When compared to pre-intervention, patients with breast cancer saw decreased total cholesterol (TC), LDL, and increased levels of poly unsaturated fatty acids (PUFAs) after undergoing radiation therapy.[29] This supports cancer treatment's influence on lipid profiles, as well as lipids playing a role in cell proliferation and apoptosis. Nutrition interventions for patients with cancer have been found to have a positive impact on body weight, nutrition status, and energy intake.[33] However, the role of nutrition interventions in altering abnormal lipid profiles in patients with cancer remains a current gap in the literature.

Since biomarkers are so extensively studied in cancer research, it is important to know how they may react with the inflammatory response to exercise or diet intervention. Finding what circulating blood levels are safest in patients with cancer, helps increase the safety and efficacy of community health interventions. Since community health interventions have shown the ability to improve patient's health, it is important to see if community nutrition programs are improving these QOL measures in patients with cancer. Because a patient's QOL can be negatively impacted by not just cancer, but also any other health comorbidities, it is important to study lipids profiles in this population as well.

Statement of the Problem

Cytokines are small proteins that are pivotal in the growth and function of the immune system. However, there is minimal research on cytokines and how they are affected by exercise and nutrition intervention in patients with cancer. Much of the research that does exist comes from controlled laboratory settings. Patients with cancer are also at risk for many toxicities, like

cachexia. This can significantly impact an individual's QOL, which can play a role in the treatment options they choose. Nutrition impact symptoms like fatigue and appetite changes can also contribute to cancer cachexia. Research has shown a lot of promise in the ability of nutrition interventions to mitigate these effects. Abnormal lipid profiles are also common in patients with cancer. However, there is little research on the effects of nutrition interventions on lipids in patients with cancer. This study seeks to gain insight into how a community-based nutrition intervention affects inflammatory blood biomarkers, QOL measures like fatigue, and lipid profiles in patients with cancer. This research focused on the inflammatory blood biomarkers TNF-α, IL-2, and IL-1β. IL-2 has already had clinical use in trying to treat cancer through immunotherapy and there has been investigation of the inhibition of TNF-α, and IL-1β as a cancer treatment. A lipid profile was taken of TC, LDL, high-density-lipoprotein (HDL), non-high-density-lipoprotein (non-HDL), triglycerides (TRG), TC/HDL ratio, and fasting blood glucose (GLU). The impact of nutrition interventions on these measures in patients with cancer is not yet fully understood and is a current gap in the literature. Further, there is little evidence on how patients with cancer receiving treatments may react to nutrition interventions. This information can be used to help determine the impact of these interventions on inflammatory blood biomarkers, QOL measures, lipid profiles, and promote future research directions.

Purpose Statement

While there is ever increasing knowledge of cytokines and their relationship with inflammation and nutrition, the effects of community-based interventions on cancer treatment outcomes are not yet fully understood. The impact of nutrition interventions on QOL measures and fatigue in patients with cancer needs further study to fully understand the role of community-based treatment and potentially prognosis. Lipid profiles also need to be studied for their

associated with cancer progression. There is also little known on the effects of nutrition intervention on lipid profiles in patients with cancer. The purpose of this research is to look at a nutrition intervention from a community health perspective and see what inflammatory, lipid, and QOL changes are occurring. This study assessed these measures pre- and post-nutrition intervention. The results can add to support of these community health programs and highlight the need for future research in this field. The findings also added to the literature on the positive effects of nutrition interventions on inflammatory blood biomarkers and lipid profiles in patients with cancer undergoing treatment. Adequate nutrition is important during cancer treatment, and this research aims to fill a gap in the literature by studying these measures and supporting the role of nutrition community-based health programs in this population.

Chapter 2. Literature Review

Cytokines are important in researching cancer immunotherapies. They have also been studied for their relationship with nutrition and inflammation. While there is not so much of a general theory related to inflammation, we have long since known that it plays a vital role in many disease processes. The scientific belief is that inflammatory mediators, such as cytokines, which persist in inflamed tissue can cause cell proliferation, survival, and growth. This modifies the differentiation status of cells forcing them into transformation. Inflammation is crucial in sustaining tumorigenesis, which is why it plays such a key role in cancer.[34] The purpose of this literature review is to look at the current research on how biomarkers relate to inflammation, cancer, and nutrition. Then look at the specific biomarkers being focused on in this intervention.

Since being discovered in the 1960s and 70s, there are now over 100 proteins labeled as cytokines. These proteins help facilitate cellular communication by acting as hormones or neurotransmitters. Cytokines function in inflammation, cellular proliferation, metabolism, chemotaxis, and tissue repair.[35] Cytokine is a broad term as many distinct types of cytokines exist. These can include interferons, interleukins, tumor-necrosis factors, chemokines, and several more classifications. Recently with the emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic there has been increased discussion of a "cytokine storm." While this term is without definition, it implies a hyperactive immune response that could be damaging to host cells. Distinguishing a normal inflammation response from a dysregulated one in a great challenge in human illness.[36] The Covid-19 pandemic has highlighted the significance of studying cytokines. This study focused on the specific cytokines IL-1β, IL-2, and TNF-α.

Tumor Necrosis Factors are another biomarker that have shown associations with cancer. TNF are a type of cytokine that can be elicited by endotoxins. Endotoxins are found in the cell wall and induce inflammation in organisms. TNFs have the ability to perform necrosis activity on tumors. It is shown to have abilities on not just mice, but also human cancer. TNF is usually produced by macrophages and T-lymphocytes.[37] TNF has a complicated role in cancer, given that through its signaling pathways it can cause cell survival, proliferation, or death. Its use in being studied and used as a cancer therapy comes from being capable of causing cancer cell death. TNF must be bound to a receptor to be expressed in immune cells. TNF can bind to two different receptors: TNF receptor 1 and TNF receptor 2. However only TNF receptor 1 is a death-domain-containing receptor, which gives it the ability to allow TNF to induce cell death.[38] TNF-α is one type of TNF that has been extensively studied when it comes to cancer.

TNF-α is an inflammatory cytokine produced by macrophages and through a receptor, such as TNF receptor 1, signals events within cells like necrosis or apoptosis. Therefore, it is mentioned frequently in fighting resistance to cancer or infections.[39] These apoptotic effects of TNF-α give it its protective properties against tumors. It is also important for tissue repair, as well as other regenerative and proliferative processes. While normal levels of TNF-α are in low serum concentrations, they increase in times of inflammation.[40] TNF-α is a protector of intracellular organisms and is the main factor in initiating an immune response to inflammation. Through its receptor's TNF-α activates macrophages that can create a feed-forward loop that creates more TNF-α. This is important for proliferation of T cells, B cells, natural killer cells, and dendritic cells. Elevated TNF-α are also important for molecule expression that allows for neutrophil extravasation. These elevated levels of TNF-α and their effect on macrophages and neutrophils partially explain the benefits of TNF-α on cancer, although at lower levels TNF-α

can relate to tumor growth.[41] This shows the complication of studying TNF-α and its relation to cancer. Another type of cytokine with a relationship with cancer are interleukins.

Interleukins are another type of cytokine prevalent in cancer research. Like TNF and Interferons, interleukins facilitate bridging the gap between the innate and adaptive immune systems and their responses. Interleukins also can play multiple roles and have pro-inflammatory and anti-inflammatory properties. These proteins bind to receptors inside the cells and react through cell growth and activation during inflammatory and immune responses. They can also function in both autocrine and paracrine systems.[42] Like TNF, using interleukins for cancer therapy has yielded mixed results. There are many different methods that have been evaluated for using interleukins as a cancer therapy. One method is through several types of engineering. One way of controlling potentially toxic effects of interleukins and other cytokines, is prolonging their half-life. Another way is interleukin-toxin fusion proteins that can attack cells with interleukin receptors, resulting in cell death. Another way interleukin's function in cancer therapy is complimenting adoptive cell therapy (ACT). Using ACT to express interleukins at the tumor site can help avoid toxicity. It can also mount a non-ACT immune response and activate tumor-infiltrating T cells. These can target cancer cells and the non-ACT immune response can activate macrophages, which are important for an innate immune response on cells without the antigen.[43] One interleukin frequently studied in cancer research is IL-2.

IL-2 is a cytokine produced by T-lymphocytes, natural killer, and DC (Dendritic Cells) cells. Its receptor affinity is with the Interleukin-2 receptor (IL-2R). IL-2R can be broken down into three subunits: alpha, beta, and gamma.[44] IL-2 and its connection to T cells is what makes it so promising to potential cancer therapies. IL-2 can induce T cell proliferation, differentiation, and activation. The purpose of this activation is to try and enhance the functional memory of T

cells.[45] Engineering IL-2 is one of the main focuses in its use in cancer research. Using methods like prolonging half-life and fusion proteins, as well as others. Bempegaldesleukin is a drug that is designed to increase the half-life of IL-2, slightly changing its receptor affinities, and reducing toxicity while increasing efficacy. This may achieve tumor regression, while activating and proliferating CD8 T cells and natural killer cells. ALKS-4230 is an engineered protein of IL-2 fused to one of its receptors IL-2R alpha inhibiting its reaction, and preferably binding to IL-2R beta gamma. This is meant to stimulate greater CD8 T cell and natural killer cell memory.[46] These interactions show why IL-2 is so pertinently studied in cancer research. Another interleukin prominent in cancer research is interleukin-1 (IL-1).

The diverse effects of IL-1 opened the door for the pleiotropic effects we know are possible of cytokines today. IL-1 has long had implications for the innate immune system and inflammation, which has only been complexed by its large extended family. Two members of the IL-1 family, IL-α and IL-β, are expressed from the same receptor but are associated with distinct functions in the body.[47] IL-1α has shown expression with cell death and from within injured tissues. This makes it a central part of inflammatory diseases. The pathogenic effects of IL-1α are not as extensively studied as IL-1β, but it has seen clinical implication for therapeutic inhibition in inflammatory disease. While IL-1α and IL-1β both are implicated in activating similar responses to produce pro-inflammatory effects, IL-α has also been detected as a precursor in healthy states, while IL-1β must undergo intracellular processing to become active. Because of this IL-1β can be thought of as a dual function cytokine and induces pro-inflammatory effects in the extracellular space. In cancer pathology IL-1α has been associated with expression aiming to reduce tumor progression early. However, IL-1α found in the extracellular environment can be associated with cancer cell survival and tumor progression. IL-1α inhibitor treatments may also

reduce symptoms of cancer toxicities like cachexia by preserving muscle loss and reducing fatigue.[48] Some studies have associated IL-1β with upregulation in many cancer types, although the subsequent effect varies. IL-1β has shown strong association with cancer cell proliferation, neo-angiogenesis, and metastasis. The full effects of cancer treatment with IL-1β inhibitors are still not fully known.[49]

Nuclear factor kappa B (NF-κB) is one transcription factor that may play a role in cytokines contributing to cancer progression. NF-κB has been shown to increase tumor proliferation and inhibit anti-apoptotic genes. This makes NF-κB a target to inhibit in some chemotherapeutic drugs.[50] The significance of this is that TNF-α for example uses NF-κB as one of its pathways. Under normal inflammation situations there is regulation from cytokines such as interleukin-10 and transforming growth factor β, as well as other hormones like cortisol. Dysregulation of these pathways can lead to sustained inflammation, often seen in patients with cancer. Allowing cytokines to play a significant role in the tumor microenvironment, often acting in favor of tumor progression. However, there is some evidence that physical activity and nutrition intervention can reduce production of pro-inflammatory cytokines and reduce cancer recurrence.[51]

Inflammatory Process and Disease

Acute inflammation is the body's response to injury or infection, and is important for repairing damaged tissues, trying to destroy foreign agents, and returning the body to homeostasis. However, imbalances that cause a weakened acute inflammatory response or an extended immune response can be detrimental. In the case of an extended immune response chronic inflammation can occur, which can damage healthy tissue if it persists.[34] This persistent

chronic inflammation can be referred to as systemic chronic inflammation (SCI). This SCI can disrupt our body's function at the cellular level, making it more susceptible to disease. One of these potential disease outcomes is tumors, as well as many other chronic diseases. SCI is also correlated with higher levels of pro-inflammatory cytokines in older populations.[52]

Because this research involved people with cancer who are currently undergoing treatment, knowing how inflammation may play a role in tumors is important. While inflammation is regulated in the acute stage, chronic inflammation is when tumorigenesis may occur. When cytokine expression becomes dysregulated it can have a pro-tumorigenic effect. In a prolonged inflammatory response, the cascade of cytokines in the tissue microenvironment is constantly enhanced, which leads to dysregulation of the auto-feedback loop. This can be due in part to the homologous and synergist effect of many cytokines and their receptors.[53] This further supports that increased levels of cytokines may demonstrate risk of tumor recurrence. Cytokines are part of the regulation of the immune response to inflammation. Some cytokines can act in an anti-inflammatory manner, helping the tissues to reestablish homeostasis. However pro-inflammatory cytokines can lead to a systemic inflammatory response syndrome, which can be self-destructive to the host. It is important to understand how cytokines react with the inflammatory response in disease to know how they may react to a nutrition intervention.

Biomarkers and Inflammation

IL-1 plays a role in both immunity and infection as a pleiotropic cytokine. However, both IL-1α and IL-1β play distinct roles in the inflammatory process.[54] IL-1α is typically found in the nucleus or cytosol. While it uses the same receptors as IL-1β, its release may be different. Following necrosis in disease the IL-1α precursor is released, and it acts as an alarmin to enact

an inflammatory cascade. Therefore, IL-1α has shown association with cancer and its inhibition has been assessed as a therapeutic.[55] We know the pivotal role IL-1α plays in the inflammatory process, because loss of IL-1 receptor antagonist function is associated with copious amounts of sterile inflammation in genetic disorders and mice. IL-1β is not present in levels of health but needs further stimulus for activation. The intracellular cysteine protease caspase-1 is required to turn IL-1β into an active cytokine. Anakinra is an IL-1 receptor antagonist that has been used in the treatment of rheumatoid arthritis.[56] The complete mechanism of IL-1β release is still not fully understood. But upon activation, if IL-1β activates IL-1R1, it can create downstream signaling such as NF-kB transcription. This leads to further inflammation and pro-inflammatory cytokine release. IL-1β has been correlated with tumor expression in breast cancer, contributing to mechanisms that increase tumor progression.[57] This TNF-α also has pro-inflammatory and anti-inflammatory properties.

What we know about TNF-α, and its pro-inflammatory properties comes from its role in disease. For example, TNF-α has shown a pro-inflammatory role in breast cancer. It is found in the tumor microenvironment, which plays a significant role in the progression of the disease.[58] Breast cancer survivors can also see cognitive impairment, which can be correlated with increased levels of TNF-α. The disease state of cancer may make the blood-brain-barrier more permeable to chemotherapy. Cytokine receptors are prominent in the hippocampus and readily cross over the blood brain barrier. This may explain the relationship between pro-inflammatory cytokines like TNF-α, reduced hippocampal volume, and impaired memory function.[59] TNF-α also has been associated with the inflammatory process.

The pro-inflammatory properties of TNF-α have been the target of many disease interventions. The blockage of TNF-α has been associated with complications like ocular

inflammation. Furthermore, TNF-α may be important in the role of antigen presenting cells and their role in regulating the immune response. Specifically, in the suppression of IL-12, another pro-inflammatory cytokine.[60] TNF-α may also act in an anti-inflammatory manner in cohesion with mesenchymal stem cells. From this study, pre-stimulation with TNF-α could improve bone marrow mesenchymal stem cells function at reducing inflammation in ocular injuries and improving corneal clarity.[61] This shows that TNF-α may have a more direct pro-inflammatory effect and shows its anti-inflammatory properties in relationship with other agents. IL-2 also has a dual role in the inflammatory process.

IL-2 is especially important in signaling pathways of controlling the pro-inflammatory and anti-inflammatory effects of T cells. IL-2 is more tailored to specific cell types, so its effects can be different based on T cell subtype. In regulatory T cells, IL-2 plays a larger role in supporting their homeostasis and differentiation, whereas in effector T cells it is more about cell growth.[62] Therefore, using IL-2 in a pro-inflammatory or anti-inflammatory manner in trying to treat disease, can be dependent on the signaling pathways. An example of the potential of pro-inflammatory effects of IL-2 is observed in metabolic inflammation and insulin resistance in obesity. In the adipose tissue increased levels of T lymphocytes that produce IL-2 may lead to increased inflammation. The increase in IL-2 can also be correlated with increased fasting blood glucose and HbA1c. Il-2 also works with other pro-inflammatory mediators like Toll-like receptors (TLRs), that contribute to its gene expression.[63] Since IL-2 and the T cell relationship can be different based on subtypes, IL-2 deficiency may play a role in regulatory T cells and inflammation. Without regulatory T cells and their contribution to autoimmunity dependent on IL-2, self- regulatory T cells and other immune cells could cause inflammation. Therefore, IL-2

immunotherapy could be beneficial in increasing regulatory T cells and reducing renal inflammation in Lupus Nephritis.[64]

These specific biomarkers can all have pro-inflammatory and anti-inflammatory properties. They are all continuously studied for their methodology and role in cancer and other inflammatory diseases. This next section of the literature review is focused on nutrition and its correlation with inflammatory biomarkers.

Nutrition, Cancer, and Cytokines

Nutrition is particularly important for those undergoing cancer treatments and for those in remission. Anemia and cachexia are both common in those undergoing cancer therapies. This can coincide with symptoms such as weakness and fatigue.[65] For cancer survivors there is definite interest from them and providers in integrating nutrition as part of patient care.[66] This study looking at ulcerative colitis patients in remission, suggests that nutrition may play a role in the cellular components of tissue in the colon. This may play a role in their risk of colorectal cancer.[67] This is important as nutrition may play a role in cancer populations and their future risk of associated cancers and treatment toxicities.

Cytokines may be important in the connection between nutrition and infection. There may be a link between malnutrition and secretion of pro-inflammatory cytokines. Because of the role of cytokines in immune response and disease, the potential for nutritional factors to influence their production is relevant. There is some potential that protein malnourishment could negatively impact cytokine production, and lead to higher rates of infection. There is not much information on the effects of fatty acid nutrition and cytokines. A small body of research suggests poly-unsaturated fatty acid supplementation may decrease cytokine production.[68]

Vitamin D deficiency is seen prevalently throughout the world. Vitamin D deficiency can interrupt T cell immune responses and the activation of T cells, macrophages and other immune secretions impacted by the expression of vitamin D receptors. In this intervention findings showed that 7.5 mg vitamin D3 injection, could lead to decreases in some cytokine levels.[69] This could be important for populations with inflammatory diseases, which being deficient in vitamin D, could lead to decreased activation of the immune cells responsible for cytokine production. This proposed intervention focuses on IL-1β, TNF-α, and IL-2, so it is important to know if there are any known effects of nutrition interventions on these biomarkers specifically.

Because IL-1's role in inflammation, diet may play a role in modulating its effects. IL-1 has been associated with fever, anemia, hepatic protein synthesis, and other inflammatory mechanisms. In weight loss the treatment of IL-1 inhibitors may account for decreased food intake, which is important due to the correlation with loss of body mass and anemia. Increased intake of n-3 fatty acids has also shown correlation with decreased serum IL-1.[70] Many patients undergo weight loss following cancer diagnosis, which can lead to increased risk for cachexia. One mechanism is that patients with cancer are found to have increased brown adipose tissue, which increases thermogenesis and the risk of catabolic wasting. Patients may also not consume enough protein, which is important for muscle synthesis.[71] Despite the correlation of individualized nutritional therapies for patients with cancer on treatment toxicities and outcomes, research is lacking on nutrition interventions that include IL-1. TNF-α is known to also play a role in the nutrition and immune system response as well.

High TNF-α levels are associated with poor outcomes in patients with cancer. This study looking at pancreatic cancer and cachexia, found higher serum TNF-α levels in those experiencing greater weight loss. These findings correlated with poor nutritional status.[72] Stress,

inflammation, and nutrition may also play a role in TNF-α levels in pregnancy. Elevated levels of TNF-α in pregnancy may be associated with insulin resistance and other poor embryonic outcomes. The findings suggest that higher stress levels could be correlated with intake of a more inflammatory diet pattern. In this case an inflammatory diet was one associated with higher intake of fatty and sugar foods. This can cause a potential increase in serum TNF-α levels, with a potential mechanism being increase in adipose tissue.[73] These findings suggest that in a nutritional intervention, looking at measurements such as body weight, body fat, and adequate vitamin intake in patients with cancer could be important for trying to show correlation with TNF-α levels. Given the correlation between high TNF-α levels and type 2 diabetes mellitus,[74] there may be relationships seen in patients with cancer or cancer survivors as well. IL-2 has also been studied with various nutrition outcomes.

The potential role of IL-2 in nutritional outcomes is not well understood. Some research suggests iron deficiency in children may play a role in the production of IL-2 by lymphocytes. This could have an impact on cell-mediated immunity.[75] This shows a potential connection between nutritional deficiencies and an impact on IL-2 production; however, this is extremely limited. Other research suggests that normal nutrition ranges are not associated with causing change in IL-2R expression and subsequent IL-2 production.[76] Like vitamin D, zinc is another vitamin whose deficiency can be shown to impair immune function by decreasing IL-2 production from T cells. From this study zinc deficiency was associated with less IL-2 expression. Chronic deficiency could interrupt zinc transporters and zinc homeostasis.[77] Although this study was in *vitro*, findings suggest that zinc supplementation may be beneficial for IL-2 production in special populations.

To summarize the findings on cytokines and nutrition for this intervention, there are several factors that may be important to look at. Body weight could be a principal factor in cachexia in patients with cancer, which could lead to increased pro-inflammatory cytokine levels. Thus, adequate caloric intake could be an important measure. Looking at extra body weight, excessive adipose tissue could lead to increased pro-inflammatory cytokine secretion. This could lead to impaired insulin resistance and affect patients with type 2 diabetes mellitus in comorbidity with cancer. There are several vitamins whose adequate intake may be important for immune system function. Vitamin D, zinc, and poly-unsaturated fatty acid deficiency may lead to increased levels of pro-inflammatory cytokines. Another concern is the inflammation level of the diet itself. Avoiding diets high in fatty or sugary food, could decrease levels of inflammation and pro-inflammatory cytokine secretion. Inflammatory biomarkers may also be useful in assessing nutritional status, which is associated with patient outcomes. While the literature is limited, the data that exists shows that proper nutrition education and intervention could be beneficial for outcomes in cancer populations and to further understand the relationship between nutrition and these biomarkers.

Quality-Of-Life and Cancer

What qualifies as QOL for patients with cancer can be very subjective. It can typically be grouped into different categories such as; physical and functional well-being, emotional well-being, social functioning, and occupational well-being. Measuring QOL can be used to assess for supportive needs for cancer-related side effects, as well as a prognostic indicator.[78] Cancer can be demoralizing to patients' psychological well-being. For instance, patients with 82.3% lower QOL scores, depression, fear of social functions, fear of cancer recurrence, income status reduction, and dissatisfaction with body image all contributed to decreased psychological well-

being.[79] Patients' physical well-being is also important to maintain. Significant weight loss, malnutrition, and cancer cachexia can all contribute to poor physical well-being. Handgrip strength has recently been added in the criterion for cancer cachexia and sarcopenia. Handgrip strength has been associated with cancer mortality as a negative predictor across different cancer types and sex. Handgrip strength may also be useful when paired with poor nutritional status, another negative predictor of cancer mortality.[80-81] Quality-of-life measures in patients with cancer can also be influenced by nutrition interventions.

Lipid Panel and Cancer

Abnormal lipid profiles have been studied as a potential risk factor for cancer. Lipids in cancer cells play a role in cell proliferation and signaling. There is concern abnormal lipids metabolism may play a role in cancer progression.[82] HDL-c has shown an inverse correlation with the risk of breast cancer.[83] However, other research has found no association between breast cancer risk and dyslipidemia. This may also depend on the severity of breast cancer.[84] Another consideration is that many of those diagnosed with cancer already live with multiple comorbidities. Comorbidities can influence the timing and potentially delay cancer diagnosis. From this study around half of those with a long-term health condition at time of diagnosis had multiple comorbidities. The risk of multiple versus a single comorbidity also increased with age.[85]

Research Questions

Research Question 1: Are cancer-related biomarkers affected in patients with cancer after undergoing nutrition education and intervention?

Research Question 2: Are lipid profile biomarkers affected in patients with cancer after undergoing nutrition education and intervention?

Research Question 3: Are cancer related QOL measures affected in patients with cancer after undergoing nutrition education and intervention?

Hypotheses

Hypothesis 1: Given nutrition intervention and education, patients with cancer will see improvement or no change in their cancer-related biomarkers.

Hypothesis 2: Given nutrition intervention and education, patients with cancer will see improvement or no change in their lipid profile biomarkers.

Hypothesis 3: Given nutrition intervention and education, patients with cancer will see improvement or no change in their cancer-related QOL measures.

Study Significance

Not only is cancer a huge problem affecting millions of people, but there is more knowledge needed to improve treatment and patient outcomes. This study adds to the literature of nutrition interventions and cancer-related biomarkers. Much of the research on nutrition interventions in cancer populations also comes from lab-controlled studies. This study adds to the literature on how community health programs are affecting these biomarkers. There is also a lack of research on how nutrition interventions affect a cancer population receiving current treatment. Considering treatment toxicities such as cachexia in this population, this research is important for demonstrating the role nutrition can play in mitigating these side effects. Quality-

of-life is also significantly impacted by cachexia and other cancer-related symptoms like fatigue. Abnormal lipid profiles in patients with cancer can also contribute to QOL measures. This research not only significantly adds to that literature in this population, but could also add to support of current cancer dietary recommendations.

Chapter 3. Method

The nutrition intervention for this study came from a local community-based nutrition program, named Cuisine for Healing. Cuisine for Healing provided the meals and nutrition education for the participants. Participants participated in a blood draw and answer health questionnaires pre- and post-intervention. Questionnaires were used to assess participant's cancer-related QOL measures. A finger stick was used to assess lipid profile numbers. Blood specimens were measured to analyze participants' blood serum levels of IL-1β, IL-2, and TNF-α.

Participants

Participants for this study were people with a cancer diagnosis that are currently undergoing some form of treatment. Cancer treatment could include medications, chemotherapy, surgery, etc. The inclusion criteria include any race, gender, or socioeconomic status person with a cancer diagnosis, currently undergoing some modality of cancer treatment. Exclusion criteria was anyone under 18, anyone without a cancer diagnosis, anyone with a current cancer diagnosis who is not receiving treatment, or anyone currently undergoing a structured exercise or nutrition intervention. The sample size for this intervention aimed for 6 participants. There was no control group. Participants were supplied meals paid for by Cuisine for Healing or the study investigators. Participants may also choose to purchase additional meals themselves. Participants were acquired via a convenience sample from those beginning intervention with Cuisine for Healing. Flyers were also be distributed by Lori Henson with Cuisine for Healing. Participants may also be referred to these programs by their oncologists.

Outcome Measures

At both pre- and post-intervention visits participants were asked to complete five questionnaires. A QOL questionnaire (SF-36), Health History questionnaire, a Physical Activity questionnaire (IPAQ-short form), a fatigue symptom inventory (FSI), and a 3-day Dietary Record. The purpose of the SF-36 is to assess changes in participants' current QOL. The Health History questionnaire is used to get background information about the health of each individual participant. The purpose of the Physical Activity questionnaire is to assess current physical abilities of the patients with cancer prior to intervention. The FSI can patients' current amount and specific symptoms related to fatigue. The 3-day Dietary Record was used to form an idea of a participant's current eating habits prior or during nutrition intervention. Following completion of the informed consent and all questionnaires, finger stick and venipuncture blood samples were obtained.

For both the pre-test and post-test, all finger sticks and venipuncture blood samples were collected by qualified investigators only. To assess a lipid profile a blood sample was collected in capillary tubes following a lancet stick. Participant's lipid profiles were then measured using Cholestech LDX technology (Abbott Core Laboratory Systems, Lake Forest, IL, USA). Participant blood draws were collected via venipuncture and placed into sterile tubes. A multiplex assay was ran using MSD technology. The assay determined the levels of each cytokine being assessed by using beads. Infrared and red dyes are used by the machine to produce up to 100 distinct colors. The MSD machine assigned distinct colors to each cytokine protein. High-speed digital signal processors and software record the fluorescent signals, which allowed the MSD to use its LED/image-based technology to determine the concentration of each cytokine. By using this technology to read the beads, the data for each bead-based assay can be

produced. This is how each participant's data for the cytokines was recorded for blood serum levels.

Procedures

Prior to recruitment for this study, the TCU (Texas Christian University) Institutional Biosafety Committee (IBC) and TCU Institutional Review Board (IRB) approval was obtained. Following IBC and IRB approval, recruitment for this project was a collaborative effort. Finding participants for this study who fit the inclusion criteria was done in coordination with Lori Henson the director at Cuisine for Healing. Participants may also be referred to this community health program by their oncologists. All participants were screened via telephone interview to ensure they meet the study inclusion and exclusion criteria by one of the study investigators. Upon arrival for their appointment for baseline testing written informed consent was obtained from all participants. The investigator explained in detail all procedural information to the participants, before they sign the informed consent document. The participant was assigned a subject code to store their data that would not include any identifying information. Demographic and health history data collected was kept in a secure locked file cabinet in the locked office of the PI, Dr. Ryan Porter. Participants were instructed that their participation in this study is completely voluntary and that they may withdraw from the study at any time. To withdraw, participants were asked to inform one of the investigators that they no longer wish to participate in the study. There was no penalty for withdrawing from this study. Participants were informed that they can have as much time as needed to ask questions and have any concerns addressed prior to beginning participation in further questionnaires, finger stick, or blood draws.

At baseline testing all participants participated in a finger stick, venipuncture blood draw, and answered all questionnaires. Participants were instructed to arrive at the lab in a 12-hour fasted state via telephone or email. The time and date corresponded to 12 hours before the scheduled appointment. Upon arrival participants completed the informed consent document and all questionnaires. Following questionnaires, participants had a finger stick and venipuncture blood draws taken. Finger stick blood samples were immediately analyzed for lipid profile data using Cholestech LDX technology. Venipuncture blood samples were centrifuged prior to proper storage for future analysis. After baseline testing took place participants began participation in the Cuisine for Healing intervention. Following completion of these intervention(s), participants participated in a post-test blood draw and again answer all questionnaires that were filled out at baseline testing. All procedures for the pre-test finger stick and venipuncture blood draw were repeated for the post-test. The duration of the study for each participant was 6-weeks. The total time expected from each participant for their participation at both pre- and post-testing, was approximately 60 minutes. Participants visited twice for the duration of the study. Enrollment was on a rolling basis, and have no firm start date. All questionnaires were filled out on paper by participants. All blood samples drawn from participants were completed via venipuncture and collected into sterile tubes by qualified investigators. Blood draws were stored safely and securely to protect confidentiality. Following collection blood draws were centrifuged to separate the plasma/serum and stored in a -80°C refrigerator in the Exercise Physiology Laboratory. Blood cytokine levels were analyzed using multiplex serum analysis with the plates being read using a Meso Scale Diagnostic (MSD) plate analyzer (Meso Scale Diagnostics, LLC, Rockville, MD, USA).

Cuisine for Healing

The nutrition intervention for this program came from meals provided by Cuisine for Healing. Participants provided meals got one meal a day for seven days of the week, giving them a total of seven meals a week. Participants typically pick up their meals for the week on Thursday. Participants may eat multiple meals in one day, or eat the average of one per day. They can also choose any meal from the menu; whether it is breakfast, lunch, dinner, or snack item. Participants may purchase meals in addition to the ones provided as a part of the study, and may therefore have a varying number of meals. The meals were organic, anti-inflammatory and high in antioxidants in nature. Participants also received some form of nutrition education. This education was focused on helping them learn what is best for them to eat when they are making their own meals. This could include help with grocery shopping or making their own meals at home. Analyzing QOL measures, lipid profiles and inflammatory biomarkers following nutrition intervention helped add to the support of these programs as part of a comprehensive rehabilitation plan for people with cancer.

Data Analysis

The design for this intervention included a pre-test and post-test. There was no data collected during the course of the nutrition intervention. A paired t-test was used to make comparisons between the pre- and post-participant cancer-related QOL measurements. A paired t-test was also used to make comparisons between pre- and post- lipid profile outcomes (TC, HDL, LDL, TRG, non-HDL, TC/HDL ratio, and GLU.), and blood serum biomarker levels (IL-1β, IL-2, and TNF-α). This answered the hypotheses that those undergoing a nutrition intervention and education would see a decrease or no change in their cancer related QOL

measurements, lipid profiles, and blood biomarkers. All data was be analyzed using SPSS Statistics.

Chapter 4. Results

A total of 6 (n=6) participants completed baseline testing for this study. Participants' baseline characteristics can be seen in Table 1. The mean age of participants in this study was 55.83 ± 12.35 years. The mean height was 170.17 ± 10.52 cm, and the mean weight was 86.5 ± 29.41 kg. There were 5 female participants and 1 male participants. One female participant dropped out for an unknown reason after baseline testing. As shown in Table 1. participants at baseline were from different racial and ethnic backgrounds. Individuals of White, African American, and Hispanic/Latino origin were included in this study. Individuals were from different socioeconomic backgrounds with 3 participants (50%) reported making 40K or less, while the other (50%) all reported making 100K or greater. At baseline participants also had a range of physical activity levels. While no participants reported being sedentary, 4 reported light levels of physical activity at baseline.

Table 1. Baseline Participant Characteristics

Variables	**Total n= (6)**
Age (years)	
18-30	0
31-40	1
41-50	1
51-60	2
61-70	1
71-80	1
Sex	
Male	1
Female	5
Race/Ethnicity	
African American	2
Asian	0
White	2
Hispanic/Latino	1
Other	0
Income Level	
<20K	2
20-40K	1
40-60K	0
60-80K	0
80-100K	0
100-150K	1
>150K	2
Physical Activity Level	
Sedentary	0
Lightly Active	4
Moderately Active	1
Extremely Active	1
	Mean
Height (cm)	170.17
Weight (kg)	86.5

Cytokine Data

Baseline and 6-week mean blood serum cytokine levels of the participants can be seen in Table 2. Blood samples were not able to be obtained via venipuncture for participants D02 and D04 at baseline or for D04 at 6-weeks. D05 and D06 have not yet returned for their 6-week follow up visit. For participant D03 no significant difference between IL-2 and TNF-α was seen between baseline and 6-weeks at $\alpha = .05$. Blood serum levels of IL-1β were not detectable in any participants and thus excluded from analysis. However, this can be relevant in that it may represent low levels of this inflammatory cytokines in this population.

Table 2. Mean Serum Blood Cytokine Levels

Participant ID	Bsl:IL-2	6W:IL-2	Bsl:TNF-α	6W: TNF-α
D01	3.037	-	1.100	-
D02	-	0.253	-	1.101
D03	0.536	0.695	1.156	0.993
D04	-	-	-	-
D05	2.609	-	0.863	-
D06	0.475	-	1.239	-

Bsl-Baseline, 6W-Six Weeks, IL-2-Interleukin-2, TNF- α-Tumor Necrosis Factor- α.

Lipid Panel Data

The mean and standard deviation cholesterol panel outcomes for the four participants in which baseline and 6-week data was collected are shown in Table 3 and Figure 1. There were no significant differences between any lipid panel markers between baseline and 6-weeks, at $\alpha = 0.05$. However, positive trends in increased mean HDL, and decreased TC, LDL, and non-HDL cholesterol were observed. Figure 1 demonstrates that 3 (75%) of participants saw a decrease in their LDL or TC/HDL ratio from baseline to 6-weeks. While there were mixed results in baseline and 6-week TRGs, 3 (75%) of participants saw a decrease or no change in their non-HDL at 6-

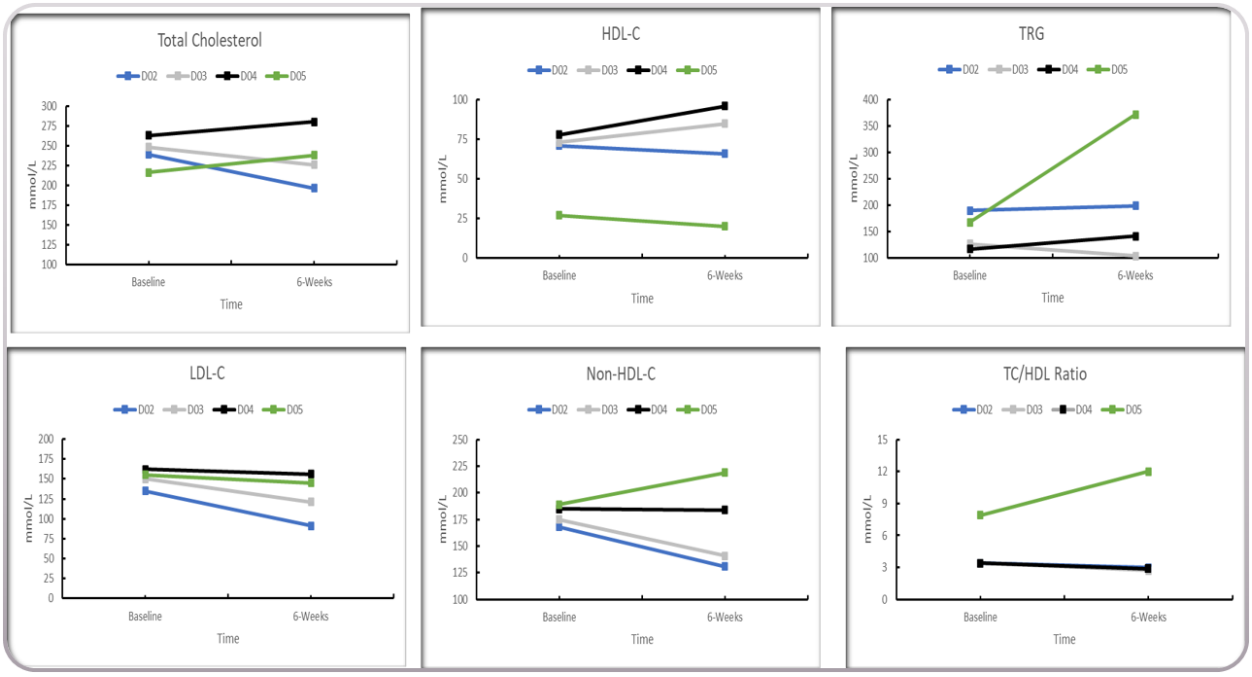
weeks compared to baseline. There was also an increase in HDL seen in 2 (50%) of the participants from baseline to 6-weeks

Table 3. Lipid Panel Measurements at Baseline and 6-weeks.

Variable	Mean	Total (n=)	Std. Deviation	Std. Error Mean
TC_Bsl	241.50	4	19.672	9.836
TC_Six	235.00	4	34.814	17.407
HDL_Bsl	62.25	4	23.684	11.842
HDL_Six	66.75	4	33.540	16.770
TRG_Bln	149.50	4	34.356	17.178
TRG_Six	203.25	4	118.452	59.226
LDL_Bsl	150.50	4	11.446	5.723
LDL_Six	128.25	4	28.814	14.407
NonHDL_Bsl	179.25	4	9.535	4.768
NonHDL_Six	168.75	4	40.631	20.316
HDLTC_Bsl	4.525	4	2.2500	1.1250
HDLTC_Six	5.150	4	4.5684	2.2842
GLU_Bsl	94.25	4	6.994	3.497
GLU_Six	99.50	4	4.435	2.217

Bsl-Baseline, Six-Six Weeks, TC-Total Cholesterol, HDL-High-Density-Lipoprotein, TRG-Triglycerides, LDL-Low-Density-Lipoprotein, Non-HDL-Non-High-Density-Lipoprotein, HDLTC-Total Cholesterol/High-Density-Lipoprotein Ratio, GLU-Fasting Blood Glucose.

Figure 1. Pre- and Post- Participant Lipid Panel Markers, (n=4).



HDL-C-High-Density-Lipoprotein, TRG-Triglycerides, LDL-C-Low-Density-Lipoprotein, Non-HDL-C-Non-High-Density-Lipoprotein, TC/HDL Ratio-Total Cholesterol/High-Density-Lipoprotein Ratio

Quality-of-Life Data

No significant changes were seen from baseline to 6-weeks in any QOL or fatigue outcomes that were analyzed using the SF-36 and FSI respectively. This included no significant decreases in health limiting activities. QOL measures on fatigue can be seen in Figure 2a and 2b. Figure 2a shows the scores for disruption index, which looks at fatigue impacting physical and social activities. Figure 2b represents a global score encompassing the entire questionnaire. While scores had no significant group change from baseline to 6-weeks, several participants saw decreased global and disruption index scores from baseline to 6-weeks.

Figure 2a and 2b. FSI Questionnaire Measures Comparing Individual Participants from Baseline to 6-weeks, (n=4).

Figure 2a.

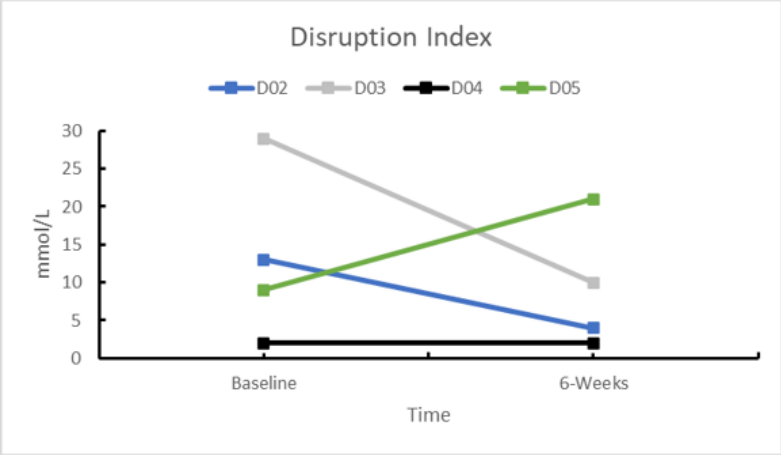
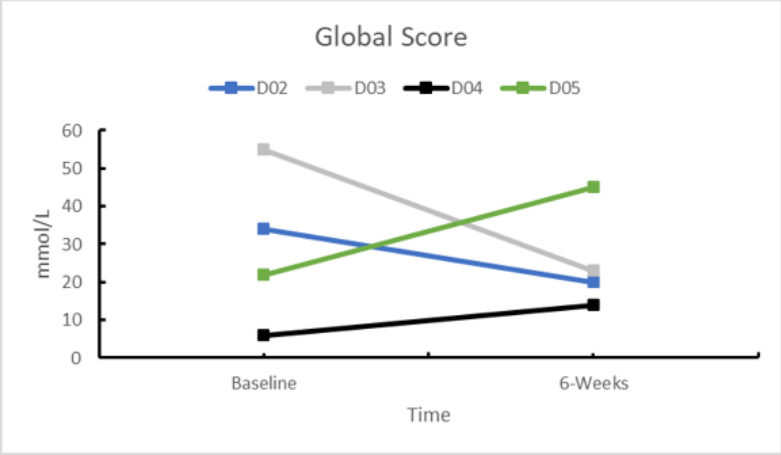


Figure 2b.



Chapter 5. Discussion

While there has not yet been sufficient data collected to statistically analyze cancer-related biomarkers, this study did supply key findings that are purposeful for future research. These findings also help support the perceived benefits participant's get from community-based nutrition programs. While there was no significant weight change for participants between the baseline and 6-week timepoint, the lack of weight loss may be beneficial considering that significant weight loss can be a symptom contributory to cachexia, which is associated with worse cancer outcomes.[21-22] There was also no significant weight gain from any participant. It is possible that the provided meals and nutrition education from Cuisine for Healing, helped participants maintain adequate caloric intake.

While no significant changes were noted, there were several positive trends in the lipid profiles of participants. Several participants saw increases in their HDL and TRG. Two participants had increased total TC, numbers, but this was likely due to increases HDL. This is supported by the fact that all participants saw decreases in their LDL, non-HDL, and TC/HDL ratio. There were no significant changes to be noted in the participant's fasting blood glucose numbers. While no significant lipid panel results occurred, looking at some of these trends can be beneficial. Prior research has shown that HDL may have an inverse relationship with the risk for breast cancer.[83] No significant decreases in HDL and some positive trends showing increased HDL, can be seen as a positive for those going through this community-based nutrition intervention. No significant increases in TC, LDL, or non-HDL cholesterol are also important, because research has shown abnormal lipid metabolism may contribute to tumor progression in pancreatic cancer.[82]

Quality of life measures assessed using SF-36 provided no significant results when participants self-reported their current health status and their health status as compared to one year prior. The lack of significant results can also be seen as a positive, in that no participant reported a significant decline in health status at 6-weeks compared to baseline. Additionally, when comparing health limiting activities from baseline to 6-weeks, no significant changes were reported. It is important to study QOL measures in patients with cancer, as it not only influences physical and cognitive health,[23] but it also can impact the treatment options patients have and the treatment options they choose.[24] It should be noted however, that this finding may simply be due to several participants from this study reporting very little to no limitation at baseline. While there was also no significant difference in problems at work or daily activities as a result of emotional problems, there was some positive change noted in one participant at 6-weeks compared to baseline. Additionally, no significant changes were reported in participants physical health or emotional problems related to social activities. This is important because prior research has shown that anxiety over cancer-related symptoms may decrease the social events that a patient may choose to attend, thereby potentially impacting emotional health.[28]

Unfortunately, while not significant, several participants did note slightly higher amounts of bodily pain in the past four weeks compared to baseline. However, the amount that this pain interfered with work or housework was minimal. When asked about how they had been feeling in the past four weeks in terms of energy level, pep, happiness, etc., there were no significant changes to be noted from the participants. Overall, no significant decrease in physical or emotional health can be seen as a positive. It is important that those engaged in a structured nutrition program are maintaining their health and well-being. Prior research on community-

based health interventions has shown that engagement, not only increases adherence to programs, but also improves patients' health outcomes.[10]

Fatigue symptom inventory results were not significant between baseline and 6-weeks. However, several participants showed decreased overall symptoms of fatigue. Two participants also reported lower fatigue disruption index scores, meaning that fatigue had less impact on their physical and social activities. This is important because of the impact of fatigue on an individual's social, physical, and emotional health.[23] The trend in fatigue may also be associated with nutritional intake. If so, it is possible that those participating in the dietary intervention had improved nutritional intake as a result of consuming Cuisine for Healing meals and applying the healthy diet principles learned through this program. This would support the already existing evidence for the benefit of nutrition programs for patients with cancer.[22]

Limitations

As a pilot study there are several limitations to report. First, the sample size was small with four participants. While it was beneficial to have participants from multiple socioeconomic and ethnic backgrounds, it means the results of this study cannot be generalized to any specific socioeconomic or ethnic group. There were also participants with multiple different cancer types included in the study. Therefore, the results cannot be generalized to any specific cancer type. Additionally, while participants were supplied meals from Cuisine for Healing, dietary and QOL data was self-reported. This means that it is possible some participants did not fully understand a QOL measure question, even if it was explained to them thoroughly. Participants may also have failed to report all foods they ate on a given day in the dietary record, as previous research has demonstrated underreporting with self-report dietary instruments.[86] The fact that participants still

reported positive trends in QOL measures, it is important given that adherence plays a large role in the success of community-based interventions.[9] The 6-week duration of this study may also limit the results as greater change might be observed in studies longer in duration. While the shorter duration of the study is important for showing positive data trends, a longer study duration would increase the significance of the results. Lastly, there was an inability to get blood via venipuncture from all participants. This limited the number of participants that could be included in cytokine analysis. The downside to this is that this study was not able to provide adequate pre- and post-analysis of inflammatory cytokines in this population.

Summary

This study looked at a community-based nutrition intervention in a cancer population. Overall, while no significant changes were seen, the results of this study showed positive trends of decreased self-reported fatigue, decreased health limiting activities, decreased lipid panel markers like LDL, and TC/HDL ratio, as well as increased HDL. These results can be used as preliminary evidence to support further studies that investigate the use of community-based nutrition interventions for people with cancer. Future research can be focused on larger studies that can include longer interventions, and look at more specific populations regarding cancer type, sex, or ethnicity.

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